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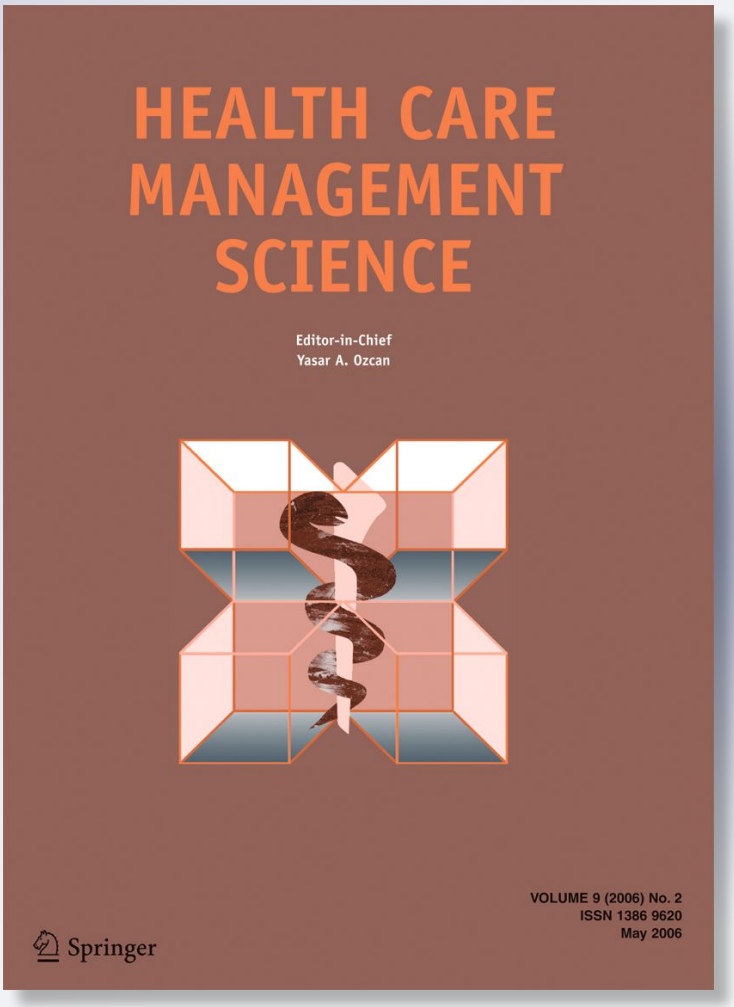

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Abstract Pandemic influenza is an international public health concern. In light of the persistent threat of H5N1 avian influenza and the recent pandemic of A/H1N1swine influenza outbreak, public health agencies around the globe are continuously revising their preparedness plans. The A/H1N1 pandemic of 2009 demonstrated that influenza activity and severity might vary considerably among age groups and locations, and the distribution of an effective influenza vaccine may be significantly delayed and staggered. Thus, pandemic influenza vaccine distribution policies should be tailored to the demographic and spatial structures of communities. Here, we introduce a bi-criteria decision-making framework for vaccine distribution policies that is based on a geospatial and demographically-structured model of pandemic influenza transmission within and between counties of Arizona in the Unites States. Based on data from the 2009–2010 H1N1 pandemic, the policy predicted to reduce overall attack rate most effectively is prioritizing counties expected to experience the latest epidemic waves (a policy that may be politically untenable). However, when we consider reductions in both the attack rate and the waiting period for those seeking vaccines, the widely adopted pro rata policy (distributing according to population size) is also predicted to be an effective strategy.

Keywords Pandemic influenza · Vaccine distribution · Mathematical modeling · Policy-decision making

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1 Introduction

In June 2009, the World Health Organization (WHO) declared a pandemic caused by a new strain of influenza A/H1N1 virus. This announcement triggered planned pandemic responses in the United States (US) and around the globe, including large-scale vaccination campaigns. Vaccination is the most effective public health intervention strategy against many infectious agents, including the influenza virus and it not only directly protects those who have been vaccinated, but also reduces transmission and thereby also indirectly offers protection against unvaccinated individuals [6, 8, 12, 18, 24, 33]. However, when the novel 2009 A/H1N1 virus emerged, the existing vaccines were not effective against the new strain and there was minimal pre-existing immunity in the human population, e.g. some cross immunity from prior exposure to similar strains in the elderly population [25]. During the six months leading up to the initial distribution of an effective 2009 A/H1N1 vaccine, the primary public health interventions included various social distancing and hygiene measures including sporadic school closures and antiviral treatment. Several studies have shown that non-pharmaceutical interventions (NPI's) alone (without antiviral medication or mass vaccination) are temporary fixes, leaving the population vulnerable to future waves of transmission once lifted [7, 9, 12, 13, 19]. However, both

NPI's and antivirals can effectively delay transmission until vaccine doses become available [3, 8, 15, 22, 23]. School closure, a community mitigation policy, is particularly controversial because of associated social and economic costs [3, 10].

When pandemic vaccines become available, policy makers face the challenge of quickly and effectively distributing them to their constituent communities to maximize the public health benefit [27]. During the 2009 A/H1N1 pandemic, the first doses became available in October 2009 in the US, six months after the index case and well into or after the major wave of transmission in most communities. In the US, for example, the release of pandemic vaccines was staggered with availability to 6.66% of the population by October 2009, and to almost 50% by February 2010.

The distribution of such limited and critical medical resources across multiple communities is a challenging operational and policy problem, not only in the United States, but all over the world. By the time the first vaccines were distributed in 2009, an estimated 10% of the population was infected in the US and thus had been naturally immunized against re-infection. Although such individuals usually no longer benefit from vaccinations, identifying and excluding such individuals from vaccination may be practically and ethically difficult. Furthermore, demand for vaccines may vary unpredictably and be correlated with local influenza activity and/or age-specific perceptions and fears [16, 31] and a mismatch between demand and supply may cause social unrest [27].

The severity and contagiousness of influenza varies considerably among strains. For example, the 1918 flu pandemic was notoriously severe, with case fatality rates (CFR) estimated around 2% [5]; the 2009 A/H1N1 was relatively mild, with an estimated average CFR of 0.159% in adults [26]. For any given influenza strain, transmission and mortality rates also differ among age groups [2, 26]. If severity and transmission are not strongly correlated, intervention strategies that effectively reduce mortality may be different than those that reduce prevalence [12]. Thus the design of intervention policy should carefully consider age-structured characteristics of the disease, the demographic make-up of the target population, and the desired outcomes of the intervention. Although there will be considerable uncertainty about the age-specific transmission and case fatality rates early in a pandemic, accurate estimates of these values are likely to become available in the months leading up to the vaccination campaign.

Prior optimization studies have shown that both deaths and hospitalizations can be minimized by prioritizing the vaccination of school-aged children (5–17), young adults (18–44), and people at high-risk of severe infections [20, 21]. It has also been suggested, that high-risk populations should be the first priority when vaccine supplies are severely limited and/or there is significant uncertainty about severity of the epidemic [2].

Here, we introduce a complementary bi-criteria decision framework for vaccine policy-making that uses a dynamic and demographically structured geospatial model of pandemic spread to forecast the effects of various vaccine distribution policies. This framework integrates critical inputs, such as early estimates of age-specific transmission and mortality rates, information about the trajectories of the ongoing pandemic in various locations, and the expected schedule of vaccine availability. It evaluates policies according to multiple public health outcomes including the expected cumulative attack rate, maximum prevalence, total mortality, while considering waiting times for vaccines. In addition, we apply our approach to evaluate several county-level vaccine distribution priorities for of the state of Arizona, based on disease characteristics and vaccine availability estimated for the 2009–2010 A/H1N1 influenza pandemic.

2 Mathematical model

We use a compartmental, age-structured and geospatial model of influenza transmission to estimate the spatiotemporal dynamics of pandemic influenza [1, 17]. The model considers multiple communities with different demographic compositions, broken into several age classes: preschool age children (0–4 years), school age children (5–19 years), adults (20–64 years) and older adults (65+ years). Disease spread within each community is modeled as an age-structured mass action model in which each age group is divided into several disease status compartments (Fig. 1). We assume homogeneous mixing within each age group and use published estimates to model mixing rates between age groups [6]. Each simulated pandemic begins with a single case introduced into an entirely susceptible population, e.g., into Yuma County, as occurred during the A/H1N1 pandemic. We analyze all possible sites of introduction (15 counties of Arizona) in addition to various transmissibility scenarios.

Specifically, within each community (i) and for each age group (j), the model tracks the changing numbers of susceptible $S_{ij}(t)$, exposed $E_{ij}(t)$, infected $I_{ij}(t)$, effectively vaccinated $V_{ij}(t)$, protected $P_{ij}(t)$, ineffectively vaccinated $U_{ij}(t)$, recovered $R_{ij}(t)$, and deceased $D_{ij}(t)$ individuals, as influenza spreads.

The dynamics are governed by the following equations, which contain disease transmission, progression and vaccination parameters defined in Table 1.

$$\frac{d\,S_{ij}(t)}{dt} = -\lambda_{ij}(t)\Omega\big(S_{ij}(t)\big) - v_{ij}(t)\Omega\big(S_{ij}(t)\big) \tag{1}$$

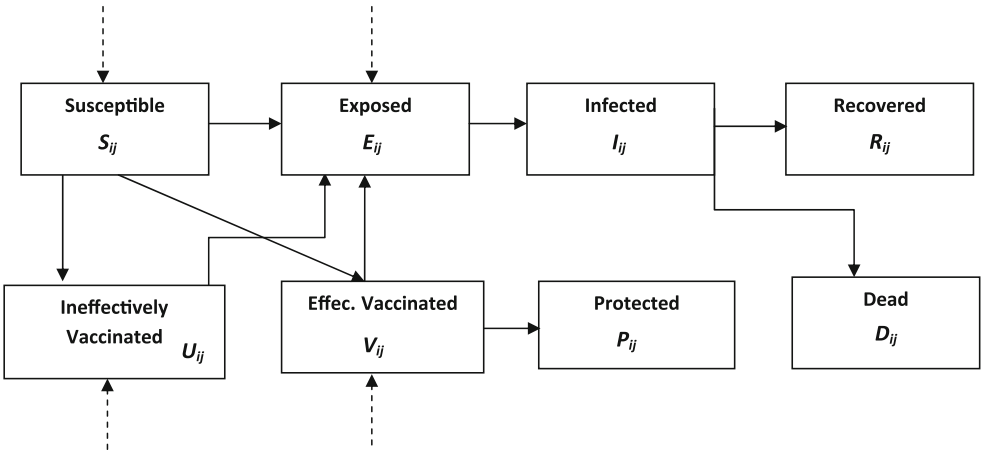

Fig. 1 Diagram of mass action model for influenza transmission within a community. In each compartment, the subscripts *i* and *j* indicate location (county) and age group, respectively. **Dashed arrows* indicate the inflow of individuals from other counties

$$\frac{d\,V_{ij}(t)}{dt} = \varepsilon\, v_{ij}(t)\Omega\big(S_{ij}(t)\big) - \eta\,\Omega\big(V_{ij}(t)\big) - \lambda_{ij}(t)\Omega\big(V_{ij}(t)\big) \tag{2}$$

$$\frac{d\,U_{ij}(t)}{dt} = (1-\varepsilon)v_{ij}(t)\Omega\big(S_{ij}(t)\big) - \lambda_{ij}(t)\Omega\big(U_{ij}(t)\big) \tag{3}$$

$$\frac{d\,P_{ij}(t)}{dt} = \eta\,\Omega\big(V_{ij}(t)\big) \tag{4}$$

$$\frac{d\,E_{ij}(t)}{dt} = \lambda_{ij}(t)\big[\Omega\big(S_{ij}(t)\big) + \Omega\big(V_{ij}(t)\big) + \Omega\big(U_{ij}(t)\big)\big] - \sigma\,\Omega\big(E_{ij}(t)\big) \tag{5}$$

$$\frac{d\,I_{ij}(t)}{dt} = \sigma\,\Omega\big(E_{ij}(t)\big) - \gamma_j I_{ij}(t) \tag{6}$$

$$\frac{d\,R_{ij}(t)}{dt} = \gamma_j I_{ij}(t) \tag{7}$$

$$\frac{d\,D_{ij}(t)}{dt} = \big(1-\gamma_j\big)I_{ij}(t) \tag{8}$$

The **Ω** terms in the equations model interactions between individuals in different communities, based on inter-community commuting patterns. We assume that only individuals in the adult age group commute. Let I be the set of communities (in this case, the counties of the state of Arizona) and let $T = (t_{i,l})$ be a symmetric matrix where $t_{i,l}$ is the total number of adult individuals in county i travelling to county l. The values of T are based on daily commuting patterns between communities [30]. We label $\Omega : R^I \to R^I$ to be the transport operator defined on the susceptible, exposed and vaccinated compartments as given in (9–12) [28]:For j=Adults

$$\Omega\big(S_{ij}(t)\big) = S_{ij}(t) + \sum_{l\in K_{\cdot,l}}\left(t_{l,\cdot}\frac{S_{lj}(t)}{N_{lj}}\right) - \sum_{i\in K_{i,\cdot}}\left(t_{i,\cdot}\frac{S_{ij}(t)}{N_{ij}}\right) \tag{9}$$

$$\Omega\big(E_{ij}(t)\big) = E_{ij}(t) + \sum_{l\in K_{\cdot,l}}\left(t_{l,\cdot}\frac{E_{lj}(t)}{N_{lj}}\right) - \sum_{i\in K_{i,\cdot}}\left(t_{i,\cdot}\frac{E_{ij}(t)}{N_{ij}}\right) \tag{10}$$

Table 1 Parameter notations and definitions

Notations and definitions of parameters	
α	*Transmission probability per contact*: Proportion of contacts between infected and susceptible individuals that lead to infection
βjk	*Age Specific Contact Rate*: Proportion of contacts of an individual in age group j occurring with individuals in age group k
λij	*Force of Infection*: Transmission rate of age group j in community i $\lambda_{ij} = \alpha\sum_{k=1}^{4}\frac{\beta_{jk}(E_{ik}(t)+I_{ik}(t))}{N_i}\forall i,(j,k)\in J$, J is the set of age groups $N_i = \sum_j N_{ij}$(see below for N_{ij})
$1/\gamma_j$	*Infectious Period*: Expected duration of infectious period prior to recovery or death
$1/\sigma$	*Incubation Period:* Expected time between initial infection to clinical onset of the disease
$1-\gamma_j$	*Case fatality rate*
$vij(t)$	Vaccination rate for age group j in county i at time t
ε	*Vaccine Efficacy*: Probability that a vaccinated individual will become fully protected.
$1/\eta$	*Vaccine pre-protection period*: Expected time between vaccination and full protection against infection
Nij	Number of people in county i and age group j

$$\Omega\left(V_{ij}(t)\right) = V_{ij}(t) + \sum_{l \in K_{.,l}} \left(t_{l,.} \frac{V_{lj}(t)}{N_{lj}} \right) - \sum_{i \in K_{i,.}} \left(t_{i,.} \frac{V_{ij}(t)}{N_{ij}} \right) \tag{11}$$

$$\Omega\left(U_{ij}(t)\right) = U_{ij}(t) + \sum_{l \in K_{.,l}} \left(t_{l,.} \frac{U_{lj}(t)}{N_{lj}} \right) - \sum_{i \in K_{i,.}} \left(t_{i,.} \frac{U_{ij}(t)}{N_{ij}} \right) \tag{12}$$

We assume, susceptible, exposed and vaccinated (both effectively and ineffectively) individuals travel, but symptomatic infectious individuals are likely to stay in their own communities and do not travel. The values in the matrix T are based on US census data regarding work-commuting patterns between counties [30], and all pairs of counties in Arizona have commuters moving between them.

3 Model parameters

In our model, we assume parameter values that are based on published estimates (see Table 2). The daily average contacts among individuals of various age groups are based on published estimates in [32]. These are the expected number of daily contacts that an individual is assumed to have in his/her own age group and also with the individuals from other age groups. School-age children have the highest contact rates and older adults (≥65) have the lowest contact rates. Other disease-specific parameters (i.e., age-specific transmission rates, age-specific mortality rates, latency period, and infectious period) are based on published estimates for 2009 A/H1N1 influenza and correspond to a reproduction number of R_0=1.4 [11, 26]. A sensitivity analysis on the basic reproduction number is also presented, by calibrating model parameters to achieve R_0=1.2, 1.6, 1.8, 2.0, 2.2, in addition to R_0=1.4. We assume a vaccine efficacy of 80% and vaccine protection rate of 10% (i.e., on average it takes ten days for effectively vaccinated individuals to be immunized) [6]. The numbers of individuals in each age group for each county in the state is based on the census data and given in Appendix A [30].

4 Vaccine distribution strategies and timing

We evaluated four strategies of vaccine distribution to the 15 counties of Arizona: (1) pro rata (simultaneously proportional to their population size): (2) sequential by population size: (3) sequential by estimated order of pandemic peaks: and (4) reverse sequential by estimated order of pandemic peaks. Our analysis takes into account the demographics of counties and the geospatial dynamics of influenza. We evaluated the efficacies of these resource allocation strategies in terms of the expected disease prevalence and mortality rates.

Pro rata This is the most common prioritization for distribution of emergency medical resources to multiple geographic locations. The available stocks of vaccines are distributed simultaneously; this policy minimizes controversy for local authorities and is thus politically favorable.

Table 2 Model parameter values and sources

Disease-related parameters					References
Transmission Probability	0.01 (R_0=1.4)				Presanis et al. [26], Fraser et al. [11]
Infectious Period	6 days (for all age groups)				Gojovic et al. [14]
Incubation Period	4 days (for all age groups)				Tuite et al. [29]
Infected Mortality Rate Values	Preschool Children 0.026%	School Age Children 0.010%	Adults 0.159%	Older Adults 0.090%	Presanis et al. [26]
Social contact parameters by age group					References
	Preschool	School-aged	Adults	Older adults	Wallinga et al. [32]
Preschool	24.16	2.54	4.93	1.64	
School-aged	2.54	32.04	7.25	2.14	
Adults	4.93	7.25	10.81	3.58	
Older adults	1.64	2.14	3.58	7.75	
Vaccination parameters					References
Vaccine Protection Rate	0.10 (for all age groups)				Chowell et al. [6]
Vaccine Supply Data	Given in Fig. 2				CDC [4]
Vaccine Efficacy	0.80				Chowell et al. [6]
Target Coverage	50%				-

However, because disease spread is dynamic and unpredictable, this policy may provide vaccines to communities unnecessarily (e.g., after a major epidemic wave) or fail to provide sufficient vaccines when needed.

Sequential by population Under this policy, vaccines are delivered to counties one at a time, in order of population size. Distribution to a given county begins only after target coverage is met in the higher priority county.

Sequential by peak Vaccines are delivered to counties one at a time, each time fulfilling target coverage before proceeding to the next county. Priority is given according to the expected timing of the pandemic peak within each county. To estimate peak times, we ran our disease transmission model 15 times, each time starting the pandemic with an index case in one of the counties of Arizona (Appendix B). For each introduction scenario, counties are then prioritized from the earliest expected pandemic peak to the latest expected pandemic peak.

Reverse sequential by peak This policy is identical to sequential by peak, except that the ordering of counties is reversed. Vaccines are distributed starting from the county expected to experience the latest peak and ending with the county expected to experience the earliest peak.

We consider several scenarios for the timing of vaccine availability. Each is a variation of the actual vaccine release schedule for Arizona during the 2009 A/H1N1 pandemic [4] (Fig. 2). During the 2009 pandemic, small quantities of effective vaccines became available approximately 150 days after the index case was infected. Additional doses became available in the ensuing weeks. Our model assumes that $v_{ij}(t)=0$ for $t<150$ and $v_{ij}(t)=v^*_{ij}(t)$ for $t \geq 150$ where $v^*_{ij}(t)$ is the rate of vaccination at time t based on the allocated vaccines to age group j in county i under the current policy and vaccine availability.

5 Model outcome measures

We consider four health outcome measures to evaluate the vaccination policies: (1) Cumulative Attack Rate (CAR), that is, the proportion of the statewide population infected during the pandemic, (2) total mortality, that is, the proportion of the statewide population that died from influenza infection during the pandemic, (3) peak prevalence, that is, the maximum proportion of the population infected at any given time during the season, and (4) average vaccine waiting time for a community. We use these outcome measures to perform decision analyses for early pandemic vaccine distribution decisions, when limited information about the spreading strain is available.

6 Results

6.1 Base case scenario

For the base case scenario (i.e., no vaccination), we assume that the pandemic begins with a single infectious school-aged individual introduced into one of the counties of Arizona (see Fig. 3 for simulated epidemic curves of the scenario with an initial case in Yuma County). Averaging across results from all 15 county-of-introduction scenarios, the model predicts a mean statewide cumulative attack rate (CAR) of 29.99% with standard deviation (SD) of 2.73, mean statewide mortality rates of 0.008%, 0.004%, 0.042%, and 0.014% in the four age groups from youngest to oldest, respectively, and an overall mean cumulative mortality of 0.028% with SD of 0.0025. The mean peak in statewide prevalence is 5.18% with SD of 0.95, occurring on average of 108 days with SD of 7.57 after the initial introduction.

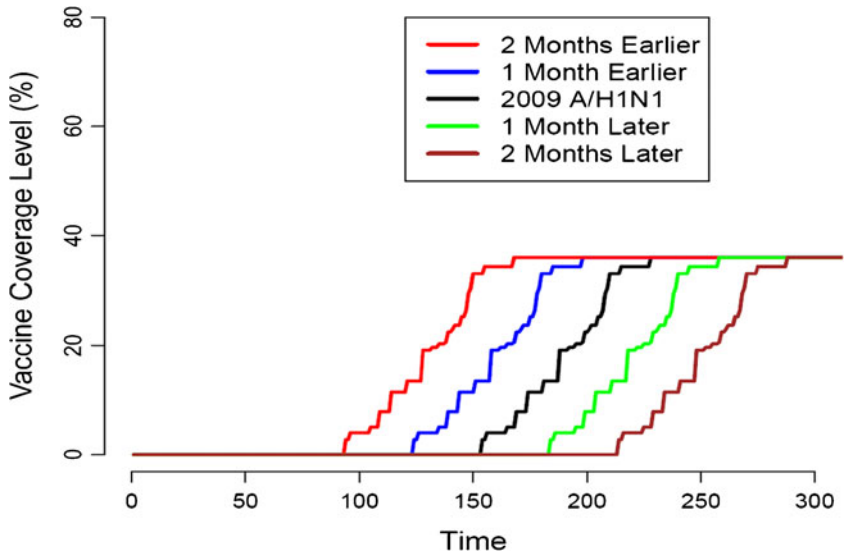

Fig. 2 Pandemic vaccine supply scenarios for Arizona. All scenarios are shifted versions of the actual vaccine availability during the 2009 A/H1N1 pandemic (*black curve*) [4]

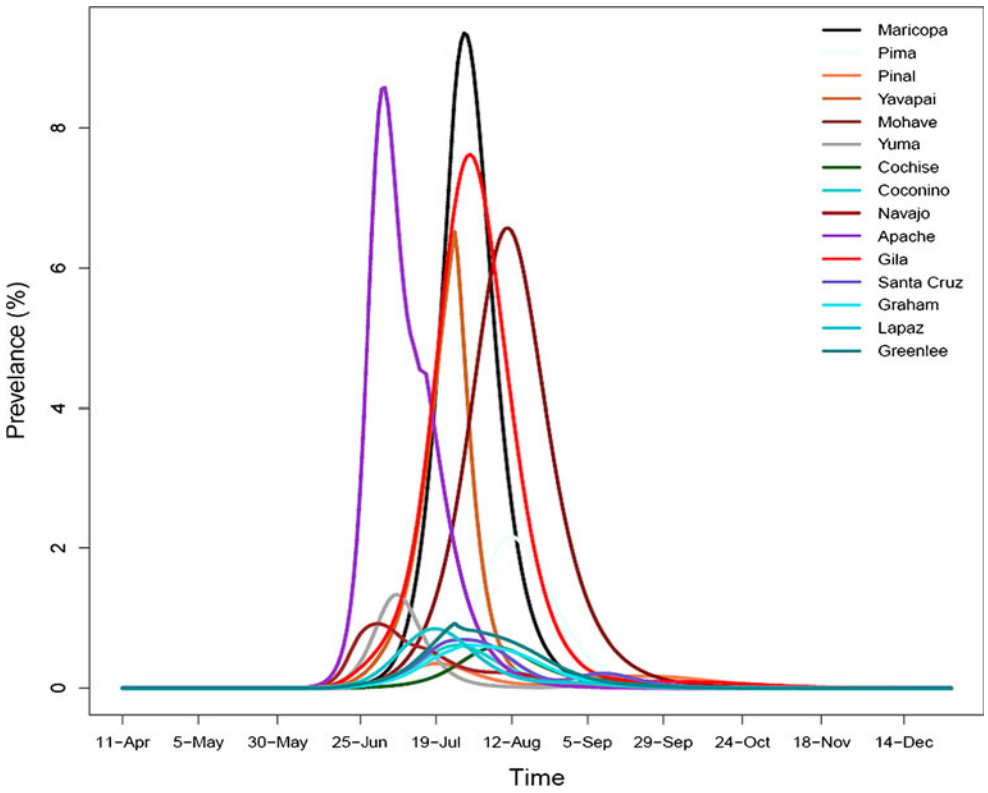

Fig. 3 Simulated epidemic time series for Arizona counties without vaccination (base case). These prevalence curves are based on an initial introduction in Yuma County and the parameters values given in Table 2

6.2 Vaccine distribution strategies

We initially report model results for each of the four vaccination policies, assuming that vaccines become available according to the schedule that occurred during the 2009 A/H1N1 pandemic, and averaging results over all 15 county-of-introduction scenarios. Figures 4 and 5 show the average age-specific statewide CAR's, mortality rates, and peak prevalence predicted for the base case and the various vaccination strategies with a R_0=1.4 as it was in the 2009 A/H1N1 pandemic.

Pro rata Dimitrov et al. [8] suggest that a pro rata distribution strategy for limited supplies of antiviral medications is close to optimal in terms of minimizing the number of cases. However, whereas antivirals are typically used only as short-term options to treat active cases of influenza or as prophylactic measuring during disease outbreaks, vaccines provide long-lasting protection. Thus, the optimal distribution strategies for antivirals and vaccines may differ. Under the pro rata vaccine distribution and for 2009 A/H1N1 transmissibility scenario, our model predicts decreases in average statewide CAR, mortality rate, and peak prevalence to 22.52% (SD 2.05), 0.0213% (SD 0.0019), and 5.01% (SD 0.92). The peak is predicted to occur, on average, 103 days after the initial infection (SD 6.43).

Sequential by population Under this policy, available vaccines are allocated to one county at a time in order of population size (from largest to smallest), covering 50% of a given county's population before proceeding to the next priority county. This policy may be highly controversial under a severe pandemic scenario, as all communities may demand access to vaccine doses as soon as they become available. The model predicts that, this strategy will reduce the mean statewide CAR to 22.98% (SD 2.10), mortality rate to 0.0218% (SD 0.0019), and peak statewide prevalence to 3.25% (SD 0.62), and cause the peak to occur, on average, 102 days after the index case (SD 6.02) for the 2009 A/H1N1 pandemic scenario.

Sequential by peak This strategy orders counties according to the expected timing of the pandemic peak and allocates the available vaccines accordingly. In this case for 2009 A/H1N1 pandemic scenario, the statewide average CAR, mortality rate, and peak prevalence are predicted to be 22.90% (SD 2.09), 0.0217% (SD 0.0018), and 3.26% (SD .60), 104 (SD 7.01) days after introduction, respectively.

Reverse sequential by peak By prioritizing counties from the latest expected peak to the earliest, we may increase the likelihood that vaccines are allocated to locations where vaccine-induced immunity can still avert a significant number of infections and deaths. Indeed, again for 2009 A/H1N1 pandemic scenario, the model predicts that this policy will lead to the largest reduction in statewide average CAR to 21.18% (1.93 SD) and mortality rate to 0.020% (SD

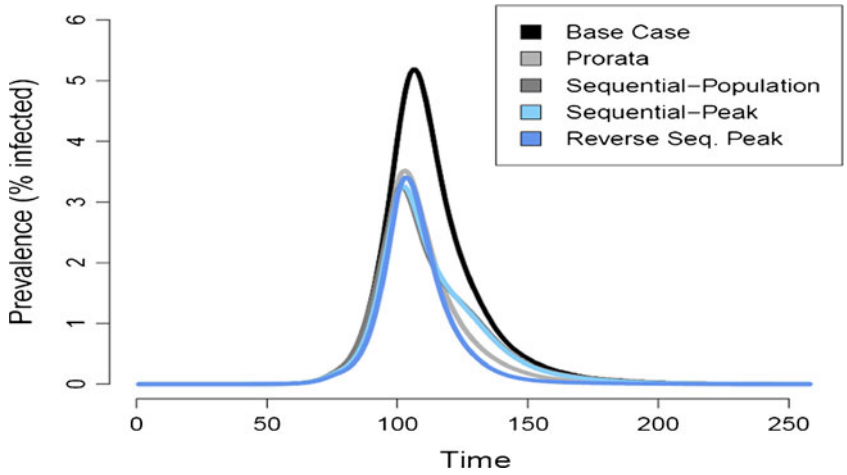

Fig. 4 Predicted epidemic curves for R_0=1.4 scenario and under the four different vaccine distribution policies: pro rata, sequential by population, sequential by peak, and reverse sequential peak. See Appendix C for predicted epidemic curves by age group

0.0018). The expected peak statewide prevalence is comparable to that estimated for the other two sequential policies (mean 3.39%, SD 0.65), occurring, on average, 105 days into the pandemic (SD 7.15).

Overall, for R_0=1.4 scenario, the reverse sequential by peak policy is predicted to achieve the largest reduction in average CAR (by 11.39%) and mortality (by 0.043%) for the whole population and also for each of the four age groups. Same result holds for all other transmissibility scenarios as well (see Appendix D). The sequential by population policy is predicted to achieve the largest reduction in peak prevalence for the population as a whole, and for the adult and preschool population. The sequential by peak policy is predicted to be most effective in reducing peak prevalence in the school age and older adult populations.

6.3 Alternative availability schedules

The development and distribution of an effective pandemic flu vaccine is constrained by manufacturing capacity, the novelty of virus, and other logistical and technological difficulties. The availability of vaccines is therefore variable and somewhat uncertain. Here, we compare the average performance of the four vaccination policies under four other distribution schedules, averaged over all 15 county-of-introduction scenarios. Table 3 compares the CAR's and peak prevalence predicted under each vaccine availability scenario for R_0=1.4.

Earlier vaccination decreases the expected CAR for each vaccine distribution strategy. The reverse sequential by peak policy is predicted to yield the largest reduction in CAR for all distribution schedules. Furthermore, our simulation

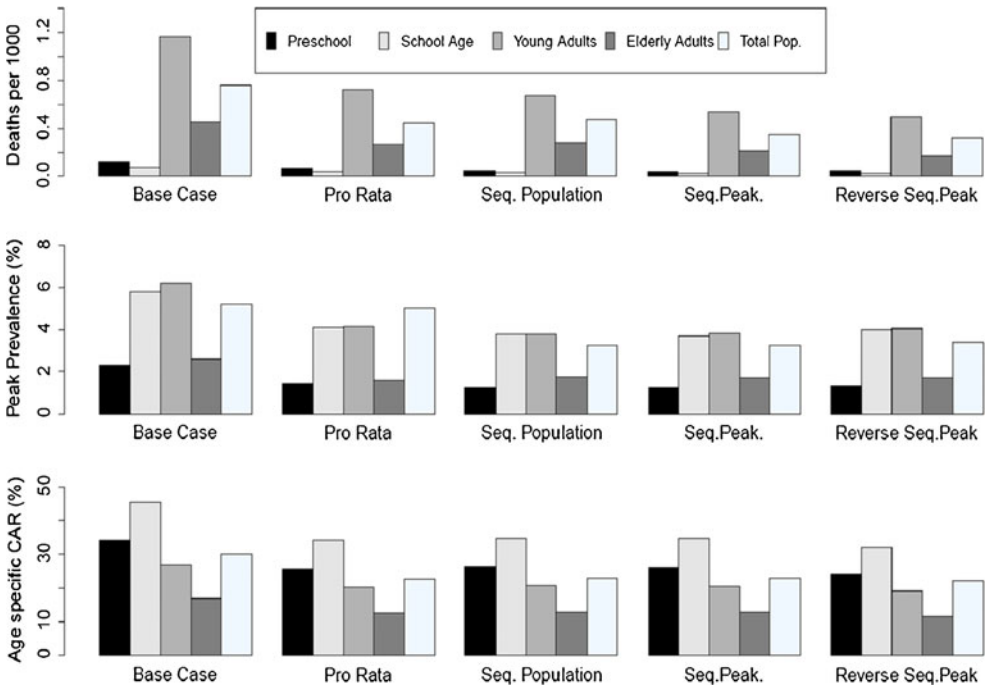

Fig. 5 Age-specific impacts of the four vaccination strategies on mortality rates (*top*), peak prevalence (*middle*), and attack rates (*bottom*). All results represent the average results of all the initial case location scenarios for R_0=1.4 (2009 A/H1N1) scenario

Table 3 Predicted impacts of vaccination policies under different vaccine supply schedules for the 2009 A/H1N1 transmissibility scenario

Schedule	Pro rata	Sequential by population	Sequential by peak	Reverse sequential by peak
Average CAR (%)				
2009 schedule	22.52	22.98	22.90	21.18
1 month earlier	17.16	16.41	17.59	15.01
2 months earlier	15.31	13.97	15.34	13.22
1 month later	22.90	23.59	23.59	22.23
2 months later	24.45	25.45	26.18	23.49
Peak Prevalence (%)				
2009 schedule	5.01	3.25	3.26	3.39
1 month earlier	4.02	3.18	3.19	3.24
2 months earlier	3.67	3.09	3.081	3.163
1 month later	5.06	3.95	3.37	3.45
2 months later	5.63	4.032	3.78	3.98

experiments show that earlier vaccination is also predicted to decrease the peak prevalence under all four policies, with the lowest peaks consistently predicted for the sequential vaccination by population policy.

7 Bi-criteria evaluation of vaccination strategies

In addition to health outcomes, decision makers are also concerned with the political applicability of various options. To address this concern, we calculate the average waiting time for vaccines under the four different policies. When $t_i(s)$ is the number of days into the pandemic that vaccines become available in county i under scenario s, p_i is the number of people living in county i, I be the set of all counties in the state, and N is the total population of the state the average waiting time for vaccines under scenario s is given by

$$T(s) = \frac{\sum_{i \in I} p_i t_i(s)}{N} \tag{13}$$

Assuming that vaccines become available according to the 2009 A/H1N1 schedule (i.e., R_0=1.4), the model predicts average waiting times for vaccines of 150, 188.76, 211.24, and 248.60 days for pro rata, reverse sequential by peak, sequential by population, and sequential by peak policies, respectively.

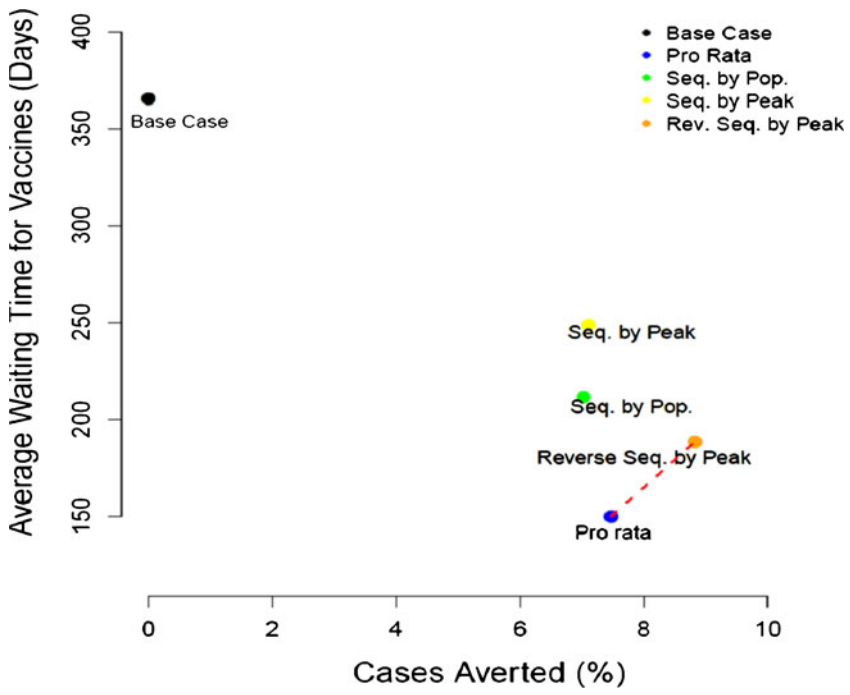

Fig. 6 Bi-criteria comparison of vaccine distribution strategies considering cases averted and average waiting time for vaccines. *Red line* indicates efficient frontier

In Fig. 6, we present a bi-criteria comparison of the four vaccine distribution policies, based on the percent of cases averted relative to the base case scenario and the average waiting time for vaccines for 2009 A/H1N1 transmissibility scenario. The pro rata and reverse sequential by peak form the efficient frontier (all non-dominated and effective strategies). This finding suggests that, of the four policies, these two policies are expected to satisfy both objectives of shortening the statewide waiting time for vaccines and reducing disease prevalence. This result holds for reproduction numbers (R_0) ranging from 1.2 to 2.2 (see Appendix D).

8 Conclusions

In this paper, we modeled four different policies for distributing vaccines to multiple communities within a state during an influenza pandemic. We assessed the impact of these policies on influenza prevalence and mortality, and sought policies that are likely to reduce the public health impact of influenza pandemic without causing long waiting times for vaccines. Our model used published, data-driven estimates for disease progression parameters, age-specific contact rates, and geographic (inter-county) movement patterns for the state of Arizona. All results are averaged over the 15 possible county-of-introduction scenarios for Arizona, and were robust across several different schedules for vaccine availability and a range of plausible reproduction numbers for pandemic influenza.

Our analyses show that if vaccines are not available until late in an epidemic, there is an advantage in prioritizing the communities that are expected to experience the latest waves of transmission. While for the epidemics considered in this paper, this strategy is expected to yield the lowest overall prevalence and mortality rates across all delivery schedules, prioritizing counties by population size is expected to cause the largest reduction in overall peak prevalence and a pro rata policy is expected to entail the shortest average waiting time for vaccines, in addition to having results close to the (presumably less politically-acceptable) alternative policies.

During the early days of an influenza pandemic, public health officials will make rapid policy decisions that aim to protect individuals while minimizing the political controversy resulting from their decisions. We demonstrate a bi-criteria decision analysis approach for balancing the two considerations (specifically expected cases averted and expected waiting time for vaccines), which can be extended to other combinations of epidemiological and socio-political criteria. Among the small set of policy options we considered, two policies—pro rata distribution and prioritization of communities expected to experience late epidemic—are predicted to balance both objectives of curbing the spread of the disease while limiting unmet demand for vaccines. Our methods can be easily extended to consider other pandemic conditions that may affect the outcome of a vaccination campaign, for example, significant amounts of age-specific cross immunity or heterogeneous use of antiviral-based and non-pharmaceutical interventions.

Appendix A

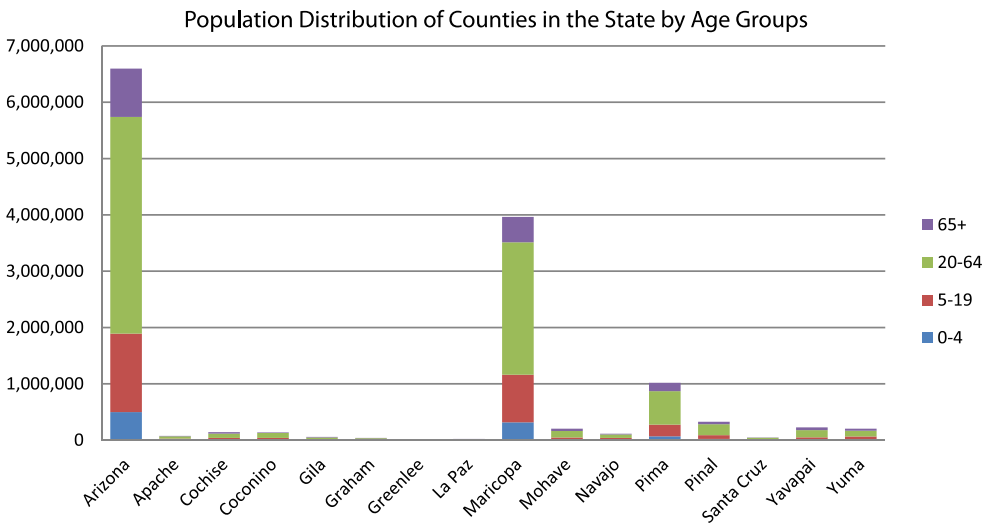

Fig. 7 Graph showing population break-down for the 15 counties of Arizona

Appendix B

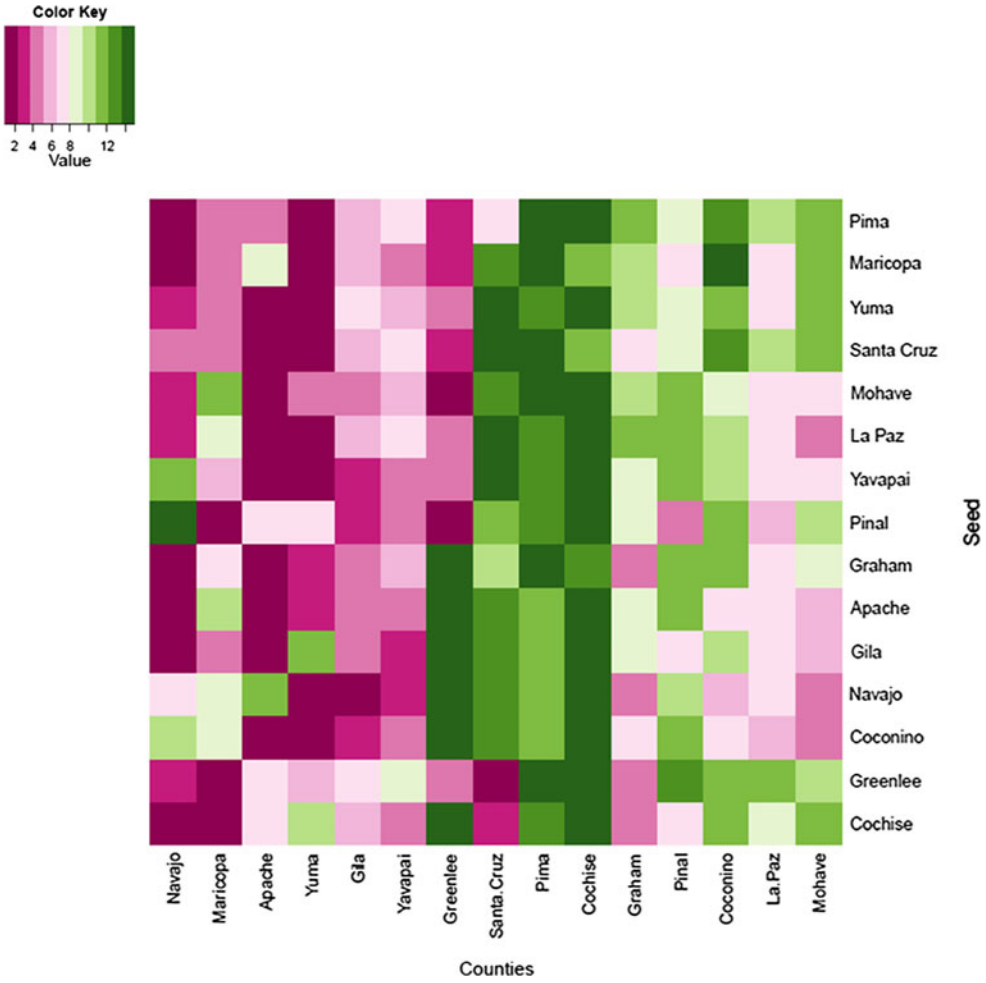

Fig. 8 Graph showing prioritization of counties based on timing of local epidemic peak. The vertical axis corresponds to the 15 different county-of-origin scenarios. Each row shows the rank ordering of counties from the one predicted to have the earliest peak (*magenta*) to the one predicted to have the latest peak (*dark green*) under the given county-of-origin scenario

Appendix C

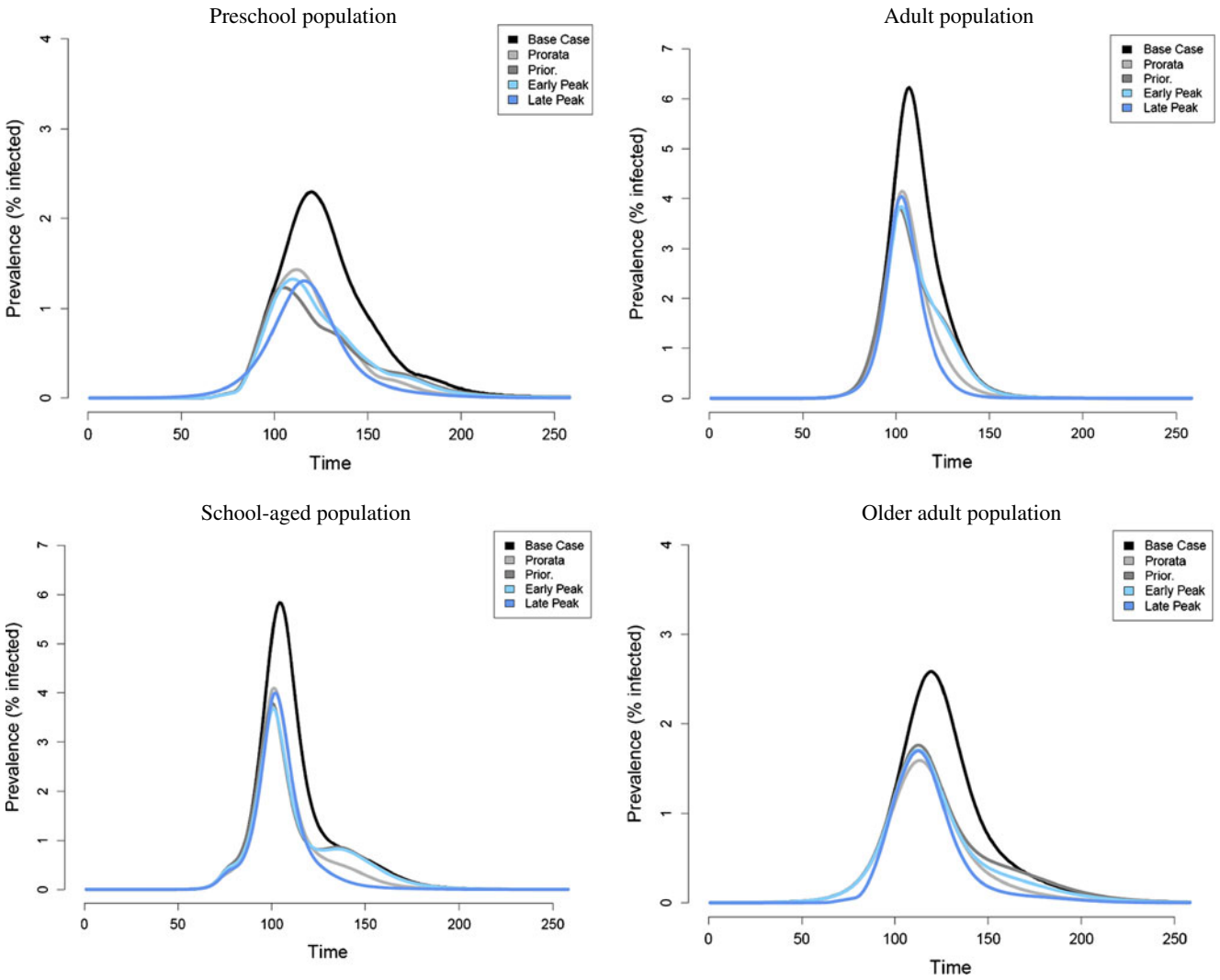

Fig. 9 Prevalence curves predicted for each age group under different vaccination policies, from youngest (*top*) to oldest (*bottom*) for 2009 A/H1N1 scenario (i.e. R_0=1.4). *C1*. Preschool population. *C2*. School-aged population. *C3*. Adult population. *C4*. Older adult population

Appendix D

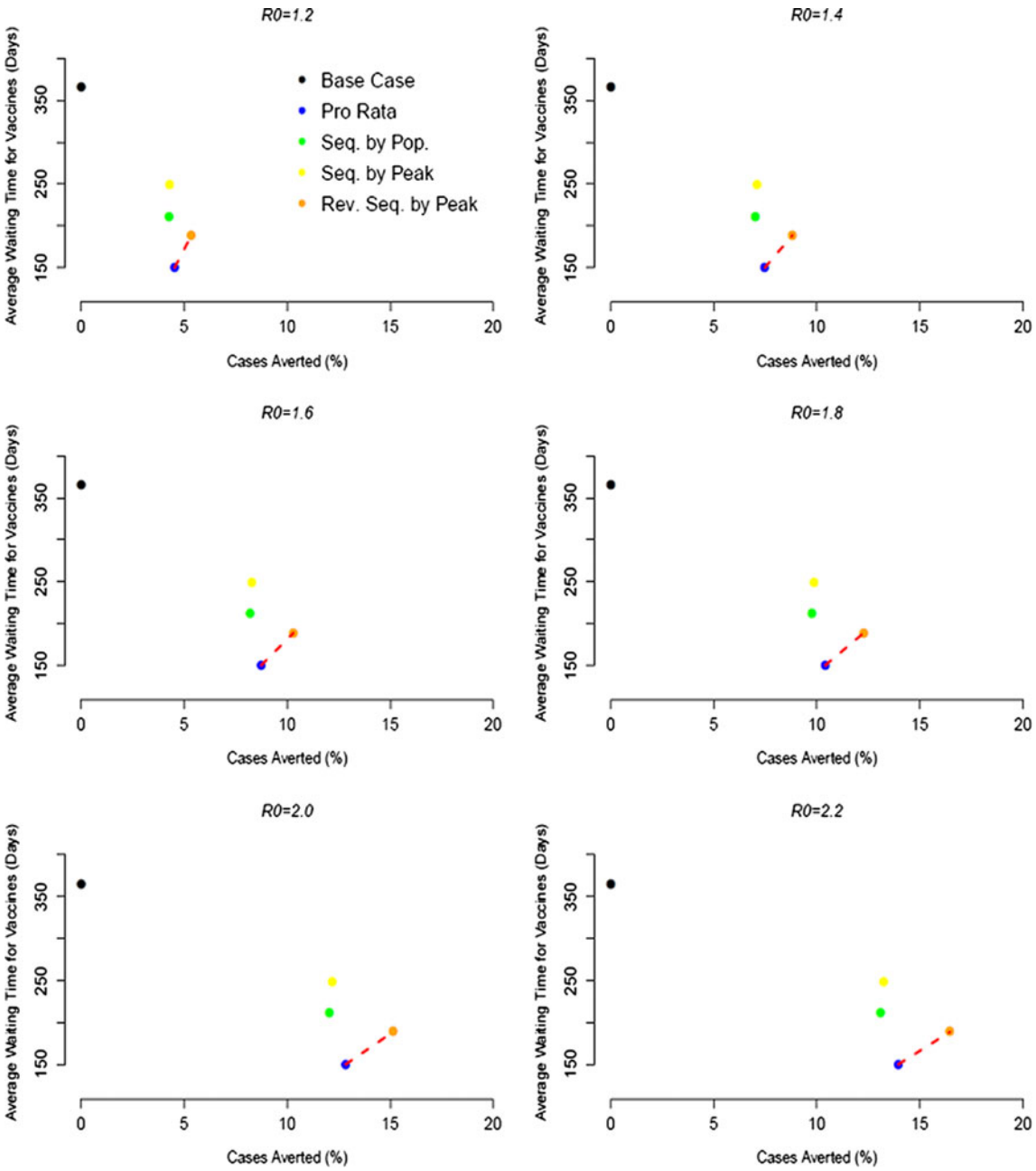

Fig. 10 Bi-criteria comparison of vaccine distribution strategies under different transmissibility scenarios (i.e., R_0=1.2, 1.4, 1.6, 1.8, 2.0 and 2.2). *Red line* indicates efficient frontiers for each scenario

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